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Acute versus Chronic Pain Experience in Alzheimer's Disease

A New Questionnaire

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Key Words
Pain · Alzheimer's disease · Questionnaire

Abstract
The low use of analgesics in patients with Alzheimer's disease (AD), compared to nondemented elderly persons, is generally explained by (1) a lower prevalence of painful conditions in the former group and (2) undertreatment of pain due to a decrease in communicative abilities in AD. However, considering the neuropathology in limbic areas in this disorder, a decline in pain affect may also explain this phenomenon. In the present study, a newly developed questionnaire was applied to 20 elderly persons without dementia, 20 patients in an early stage and 20 patients in a midstage of AD. The questionnaire includes 10 pairs of painful situations, each pair consisting of an acute and a chronic affective painful situation. It was hypothesized that, compared to controls, AD patients during the course of the disease would report to suffer increasingly more from an acute than from a chronic, affective painful situation. The results support our hypothesis. Limitations of the present study are discussed.

Patients with Alzheimer's disease (AD) are prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) and non-NSAIDs less frequently than nondemented elderly persons [1–3]. Two explanations are generally given for this phenomenon: (1) it is assumed that elderly people without dementia tend to suffer from more painful conditions than AD patients. Indeed, in some studies, the AD group showed a lower prevalence of joint pain and arthritis than the nondemented group [1, 4], although in another study a similar percentage of subjects with arthritis was found in both groups [5]; (2) pain in AD patients remains undetected due to the patients' deteriorating capacity to report it [6]. This second explanation implies that the use of analgesics depends on the stage of the disease. However, in one recent study, it was observed that the use of NSAIDs and non-NSAIDs was indeed significantly lower in AD patients than in nondemented elderly persons, but that it was independent of the stage of the disease [7].

The present study examines a possible third explanation which is derived from the neuropathological distribution in AD. The hypothalamus, the septohippocampal region and the amygdala play a significant role in the affective responses to pain [8] and are affected in AD [9, 10]. Information about affective, chronic types of pain to

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these limbic areas is transmitted by the paleospinothalamic tract [11–13]. The neospinothalamic tract which mediates information about sharp, acute pain, projects to the somatic sensory cortical areas, S-I and S-II [14]. Interestingly, the somatic sensory cortical areas are relatively well-preserved in AD [15], implying that AD patients might still be able to experience an acute painful stimulus. Consequently, one could argue that, in addition to a number of painful conditions and communication problems, AD patients suffer from less pain due to an alteration in the experience of pain affect. However, examining this assumption by the administration of regular pain questionnaires in AD might present a major problem. If the patient with one or more painful conditions experiences little pain, a number of items, including those which refer to pain affect, become superfluous. Consequently, it will be difficult to examine the extent to which a decline in pain affect contributes to the overall decrease in pain experience. Therefore, a new questionnaire was developed, including 10 pairs of painful conditions, each pair consisting of 1 acute situation and 1 chronic, affective situation. Subsequently, AD patients and controls had to indicate from which of the 2 painful conditions in each pair they would suffer most (a forced choice). The major advantage of this new instrument is that, although painful conditions may be present, the patient does not need to experience pain himself. The selected items represent such everyday painful situations that the patient should be able to imagine the degree to which he would suffer from it. Due to a decline in the sense for chronic, affective aspects of pain, it was hypothesized in the present study that, compared to controls, AD patients would indicate to suffer increasingly more from the acute painful conditions during the course of the disease.

Materials and Methods

Subjects

The sample consisted of three groups: 20 AD patients in a relatively early stage, i.e. stage 1 of the Clinical Dementia Rating Scale (CDR) [16] and stage 5 of the Global Deterioration Scale (GDS) [17]; 20 AD patients in a midstage, i.e. stage 2 of the CDR and stage 6 of the GDS, and 20 elderly persons without dementia. The three groups were not different for age, i.e. the early-stage AD patients had a mean age of 83.1 (range 72–92), the midstage AD patients had a mean age of 83.6 (range 69–91), and the mean age of the elderly persons without dementia was 86.0 (range 72–95). All subjects had completed elementary school. The various groups did not differ in gender.

All AD patients met the NINCDS-ADRDA criteria for the clinical diagnosis of probable AD [18]. Subjects were excluded from participation in this study if they had a history of psychiatric disorder, particularly depression, alcoholism, cerebral trauma, cerebrovascular disease, hydrocephalus, neoplasm, epilepsy, disturbances of consciousness or focal brain disorders. Level of cognitive functioning was assessed by using the Mini-Mental State Examination (MMSE) [19], i.e. a shortened 12-item version with a maximum total score of 12 [20]. Subjects with a score of less than 7 were classified as having serious cognitive disturbances, whereas scores ranging between 6 and 11 indicate mild cognitive deterioration. The mean MMSE score of the control group was 11.2 (range 9–12), of the early-stage AD group 6.65 (range 3–10), and of the midstage AD patients 3.1 (range 1–7). The ranges of the mean scores of the various groups showed some overlap, i.e. deviant scores were observed for 3 out of 20 controls (15%; 2 controls had a score of 9 and 1 showed a score of 10), for 7 out of 20 early AD patients (35%; 3 patients showed a score of 3, 2 patients had a score of 4 and 2 patients had a score of 6), and for 1 out of 20 midstage AD patients (5%) who showed a score of 7. Despite this overlap, the 3 controls did not show any further symptom which could possibly indicate the beginning of dementia, whereas the 7 early-stage AD patients and the 1 midstage AD patient completely met the criteria of the GDS and CDR for early- and midstage dementia, respectively. Importantly, further analyses revealed a significant difference in MMSE scores between the control group and early-stage AD patients [$t(27.43) = 8.39$; $p < 0.001$], and between early- and midstage AD patients [$t(31.99) = 6.16$; $p < 0.001$].

Questionnaire

A simple questionnaire was constructed, listing 10 pairs of familiar painful conditions (appendix). Each pair consists of an acute painful condition versus a chronic, affective condition (the acute versus chronic pain questionnaire: ACPQ). In the ACPQ, the 10 chronic painful conditions are indicated by a 'c', the 10 acute conditions by an 'a'. The patient is asked from which of the 2 conditions in each pair he would suffer the most. It is essential that the patient is not asked which of the 2 conditions causes most *pain* because then the quantitative aspects of pain (e.g. intensity) are assessed instead of the more qualitative, affective experience of the painful condition.

Instructions. The instructions of the ACPQ are as follows: 'I describe to you two familiar situations which might cause heavy burden. Even if you have never experienced a similar situation yourself, you can probably imagine what it would be like'. *Question*: 'Please indicate from which of the two following situations you would suffer most'. In view of the short-term memory disturbances in AD, it is absolutely necessary to repeat the question before presenting a new pair of painful situations.

Scoring. Both the 10 chronic, affective painful situations and the 10 acute painful conditions have a total score of 10 each. However, the patient has to chose between a chronic and an acute painful condition in each pair, resulting in two complementary scores for chronic and acute painful conditions, respectively. For the data analyses, the scores of the acute painful conditions were employed.

Reliability of the Scale. The scale has been administered to 108 subjects, including cognitively unimpaired elderly persons, nondemented cognitively impaired elderly persons and AD patients. The reliability coefficient by means of Cronbach's α (internal consistency) appeared to be 0.89.

Duration. The administration of the questionnaire will take about 5 min.

Table 1. Percentage of elderly persons without dementia and percentage of patients in an early stage and midstage of AD involving different painful conditions

	Elderly persons without dementia (n = 20)		AD patients			
			early stage (n = 20)		midstage (n = 20)	
	n	%	n	%	n	%
No painful condition	2	10	4	20		
Painful conditions						
Arthritis/arthrosis (A)	7	35	9	45	6	30
Fractures (F)			2	10	5	25
Postoperative states (P)					1	5
Miscellaneous (M)	2	10	1	5	3	15
A + F	4	20			1	5
A + P	1	5			1	5
A + M	4	20	2	10	2	10
F + P			1	5		
F + M			1	5	1	5
Total number of subjects	18		16		20	

A + F = Arthritis + fractures; A + P = arthritis + postoperative states; A + M = arthritis + miscellaneous; F + P = fractures + postoperative states; F + M = fractures + miscellaneous.

Painful Conditions

Characteristics. A possible influence of the presence of chronic pain in one group and the absence of pain in another group had to be excluded. Therefore, separate conditions which might cause pain for those with and without dementia were collected by one of the authors (E.J.A.S.) by reviewing the medical records which were composed by the former general practitioner and by the present nursing home physician. The following four categories of painful conditions emerged, i.e. (1) arthritis/arthrosis, (2) recent fractures (within the last year), (3) postoperative states (e.g. total hip), (4) miscellaneous (tendinitis and diabetes neuropathies). Also, patients who showed a combination of these painful conditions participated in this study, resulting in 9 categories of painful conditions (table 1). These painful conditions are similar to those generally observed in nursing home residents [21]. The number of subjects with a chronic painful condition did not differ between the three groups ($\chi^2 = 3.38$, d.f. = 2, n.s.). As for the nature of the painful conditions, there was a significant effect between the three groups with respect to the presence/absence of arthritis ($\chi^2 = 6.64$, d.f. = 2, $p < 0.04$). More specifically, a significant difference was observed between the control group (88%) and the midstage AD group (50%; $\chi^2 = 6.63$, d.f. = 1., $p < 0.02$), whereas the presence of arthritis did not differ between the control group and the early-stage AD group (69%; Fisher's exact: n.s.) and between the early- and midstage AD group (Fisher's exact: n.s.).

Presence of Pain at the Moment of Administration. As the presence of pain at the moment of administration might influence the subjects' selection of the presented items, the three groups were assessed on this particular point. On a 7-point scale, ranging from 0 (no pain) to 6 (a lot of pain), the subject could indicate the intensity of the pain. Data analyses revealed that, although no differences were found between the control group (M = 1.1, range 0–2) and midstage AD patients (M = 0.7, range 0–4), and between early- (M = 0.2, range 0–3) and midstage AD patients, controls, compared to early-stage AD patients, reported significantly more pain at the moment of administration of the questionnaire (Mann-Whitney U: Z = 1.96; $p < 0.05$). Importantly, however, for each group, pain at the moment of administration was not related to the responses to the pairs of items of the questionnaire.

Data Analyses

The SPSS PC program [22] was used for statistical analyses. A p value of < 0.05 was considered significant.

Results

A total score of acute painful conditions was calculated for each subject. An analysis of variance carried out on these data revealed that the total acute pain scores differed significantly between the three groups [$F(2, 57) = 191.67$; $p < 0.001$]. The mean scores for the control group, the early- and midstage AD patients were 0.25, 3.15 and 7.05, respectively. Post hoc analyses of these data showed that the total acute pain score of the control group was significantly less than that of the early-stage AD group [$t(22.32) = 8.31$; $p < 0.001$]. A similar significant difference was observed between the early- and midstage AD patients [$t(38) = 9.39$; $p < 0.001$].

Table 2. χ^2 tests of the number of controls (co) and AD patients in an early stage and a midstage (mid) selecting the acute painful conditon from each of 10 pairs of items of the ACPQ

The ACPQ questionnaire	Subjects selecting the acute painful condition			Co vs. early AD		Early vs. mid AD	
	co	early AD	mid AD	χ^2 (d.f. = 1)	p	χ^2 (d.f. = 1)	p
1 Headache/bumping your head hard	3	11	20	7.03	<0.01		<0.001[1]
2 Bite your tongue/toothache	0	3	12		<0.12[1]	8.64	<0.005
3 Having your ear pulled/earache	0	3	16		<0.12[1]	16.94	<0.00005
4 Bellyache/your toes being stepped on	1	8	11		<0.001[1]	0.90	<0.35
5 Stomachache/having your hair pulled	0	5	13		<0.02[1]	6.46	<0.02
6 Burning your finger on a match/a sore throat	1	13	13	15.82	<0.0001	0.00	<1.00
7 Pain in your knee/being hit	0	6	17		<0.01[1]	12.38	<0.0005
8 Being pinched nastily/muscle ache	0	7	12		<0.005[1]	2.51	<0.12
9 Bumping your funny bone/backache	0	4	13		<0.05[1]	8.29	<0.004
10 Pain in the neck/pricking your finger on a pin	0	3	14		<0.12[1]	12.38	<0.0005

[1] Fisher's exact.

Inspection of the separate pairs of items of the questionnaire indicates that, compared to AD patients, very few controls selected the acute painful condition (table 2). Moreover, these data reveal that the more AD progresses, the more AD patients indicated that they would suffer most from the acute painful items. Further analyses of these data resulted in significant differences between the control group and the early-stage AD group, and between the early-stage and midstage AD group for 7 out of 10 pairs of items (table 2).

Discussion

The results of the present study show that, compared to controls, AD patients indicate that they suffer more from acute painful conditions than from chronic, affective situations. Interestingly, the present findings also reveal that the more AD progresses, the higher the number of AD patients who say that the acute painful conditions are the heaviest burden.

The present results are further supported by other studies that examined the side-effects of lumbar puncture. It has been observed that demented elderly persons have less severe post lumbar puncture headache (PLPH) [23], certainly an affective, painful condition. Compared to other groups of patients, the PLPH was less frequent, less intense and its duration shorter in patients with mild-to-moderate dementia [23]. Interestingly, in another study nondemented subjects were also included. The results show that, compared to younger cognitively unimpaired subjects (age <60 years), older cognitively unimpaired subjects (age >60 years) experienced less severe PLPH [24]. However, the results further indicate that the older the subjects and the more serious their cognitive deterioration and cerebral atrophy, the lower the headache incidence [24]. Unfortunately, neither study indicates whether AD patients were included.

The present findings also match those of an earlier study in which an enhanced response to the elicitation of nociceptive reflexes was observed in AD patients [25]. Elicitation of nociceptive reflexes could be considered a patient's reaction to an acute painful stimulus.

The present study has several limitations. In the first place, AD patients might have misinterpreted the presented items in general or, more specifically, the items concerning chronic pain, resulting in a preferred selection of the items on acute pain. Arguments against this assumption are (1) in the Dutch-language version of this questionnaire, the word 'pain' occurred in each chronic painful condition which could have facilitated the AD patients' understanding and choice for this specific condition; (2) compared to the acute painful condition, the chronic painful situation could be presented in a much

shorter sentence (mainly 1 or 2 words), enabling the AD patient to understand and remember it more easily; (3) all the items of the questionnaire represent very simple, everyday painful situations, and (4) in another study, pain reports of cognitively impaired elderly persons appeared to be just as valid as those of elderly persons with a normal mental status [26]. Nevertheless, further studies on the validity of the questionnaire are necessary. In the second place, the question whether the information obtained by imagining the extent of suffering caused by a certain painful situation can be used to draw conclusions with respect to the real situation remains unanswered. Nevertheless, administration of the ACPQ may offer a better insight into the relation between the painful situation and a patient's reaction to it.

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Appendix: The Acute versus Chronic Pain Questionnaire (ACPQ)

Date of administration: _____

Name + address: _____

Date of birth: _____

Education: _____

Occupation: _____

Male/female

How much pain do you have at this moment?

0	1	2	3	4	5	6
no pain						a lot of pain

Can you indicate the location of the pain?

Instructions: I describe to you two familiar painful situations which might cause heavy burden. Even if you have never experienced a similar situation yourself, you can probably imagine what it would be like. *Question:* 'Please indicate from which of the two following situations you would suffer most'.

	Pairs of items			
1	Headache (c)* Repeat question	0	bumping your head hard (a)*	0
2	Bite your tongue (a) Repeat question	0	toothache (c)	0
3	Having your ear pulled (a) Repeat question	0	earache (c)	0
4	Bellyache (c) Repeat question	0	your toes being stepped on (a)	0
5	Stomachache (c) Repeat question	0	having your hair pulled (a)	0
6	Burning your finger on a match (a) Repeat question	0	a sore throat (c)	0
7	Pain in your knee (c) Repeat question	0	being hit (a)	0
8	Being pinched nastily (a) Repeat question	0	muscle ache (c)	0
9	Bumping your funny bone (a) Repeat question	0	backache (c)	0
10	Pain in the neck (c)	0	pricking your finger on a pin (a)	0

Total score chronic pain: _____

Total score acute pain: _____

* a = Acute painful condition; c = chronic painful condition

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